Biologicals 46 (2017) 143–147

Contents lists available at ScienceDirect

Biologicals

journal homepage: www.elsevier.com/locate/biologicals

The role of miR-17-92 cluster in the expression of tumor suppressor genes in unrestricted somatic stem cells

Rezvan Tavakoli [a], Saeid Vakilian [a], Lida Langroudi [a], Ehsan Arefian [b], Mehdi Sahmani [c], Masoud Soleimani [d], Fatemeh Jamshidi-Adegani [e, *]

[a] Stem Cell Technology Research Center, Tehran, Iran
[b] Department of Microbiology, School of Biology, College of Science, University of Tehran, Tehran, Iran
[c] Department of Clinical Biochemistry, Cellular and Molecular Research Center, Qazvin University of Medical Sciences, Qazvin, Iran
[d] Department of Hematology, Faculty of Medical Science, Tarbiat Modares University, Tehran, Iran
[e] Department of Molecular Medicine, School of Medicine, Qazvin University of Medical Science, Qazvin, Iran

ARTICLE INFO

Article history:
Received 21 November 2016
Received in revised form
2 February 2017
Accepted 8 February 2017
Available online 17 February 2017

Keywords:
Tumor suppressor gene
Tumorigenesis
microRNAs
miR-17-92 cluster

ABSTRACT

The miR-17-92 cluster consisted of seven miRNAs (mir-17-5p, -17-3p, -18a, -19a, -20a, -19b-1, and -92a-1). Previous studies have shown this cluster has been over-expressed in several cancers. The aim of this study was to evaluate the over-expression impacts of miR-17-92 on stem cells. In the current work, the effect of miR-17-92 cluster which was cloned in Lentiviral vector has been investigated on unrestricted somatic stem cells (USSCs). Tumor suppressor genes (p53, p15, RBL1, SMAD2, SMAD4, and MAPK-1) expression, especially p53, was considerably reduced. These data show the potential of miR-17-92 for oncogenesis regulation in stem cells. In conclusion, the role of miR-17-92 in USSCs may provide a better understanding of its function in tumorigenesis and for the possible use in cell therapy of the anti-mir-17-92 cluster.

1. Introduction

Micro RNAs (miRNAs) are non-coding RNAs that have critical role in biological processes. The function of these molecules is reduction of the translation and stability of mRNAs; for instance, tumorigenesis, regulation of cell cycle genes, inflammation, differentiation, response to stress and apoptosis have been controlled by miRNAs [1,2]. An increasing number of studies have shown that various cancers correlate with miRNAs, which can function as tumor suppressors and oncogenes and might have vital role in cancer progression [2,3]. For instance, researchers indicate that mir-125b-1 is correlated with lung, leukemia, breast, ovarian, and cervical cancers. Moreover, mir-15a and mir-16-1 are down regulated in B-cell chronic lymphocytic leukemia (CLL) [4]. It has been shown that mir-15a and mir-16-1 are anti-apoptotic genes which are over expressed in many types of human cancers, such as leukemia and lymphomas [5]. Extensive studies have revealed miR-143 and miR-145 are considerably diminished in colorectal tumors and expression of these miRNAs decreased in lymphoid, cervical, breast and prostate cell lines [6]. Further study, claims that miR-21 is over expressed in glioblastoma. This miRNA mediated cell growth by inhibiting apoptosis as shown by antisense studies [7]. This finding points to an oncogenic role for this miRNA.

The miR-17-92 cluster has been well-characterized as oncogenic miRNA whose abnormal expression was found in a variety of cancers and results in increased cell proliferation and diminished apoptosis. This cluster consisted of mir-17-5p, -17-3p, -18a, -19a, -20a, -19b-1, and -92a-1 which result from a single polycistronic transcript placed at chromosome13q31 [8,9]. In lymphomas and lung cancer, the overexpression of this cluster is reported [10]. Wang et al. (2012) have identified circulating miR-17-5p and miR-20a as molecular markers for gastric cancer [11]. As well as Shan and Yang (2013) have shown that mature miR-17-5p and passenger miR-17-3p stimulate hepatocellular carcinoma and induce invasion and prostate tumor growth, respectively [12].

Unrestricted somatic stem cells (USSCs) have been known as human somatic stem cells from the umbilical cord blood. High self-renewing potential without spontaneous differentiation of these cells makes them to the high capable for cell therapy and transplantation. Due to these facts, these cells have been broadly applied to examine the effect of different miRNAs on regulation of cell

* Corresponding author.
E-mail address: fjamshidiadegani@gmail.com (F. Jamshidi-Adegani).

http://dx.doi.org/10.1016/j.biologicals.2017.02.006
1045-1056/